UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,966	11/17/1999	RODERICK L. HALL	98.736-A	5234

20306 7590 07/02/2002

MCDONNELL BOEHNEN HULBERT & BERGHOFF
300 SOUTH WACKER DRIVE
SUITE 3200
CHICAGO, IL 60606

EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application N .	Applicant(s)	
	09/441,966	HALL ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 15-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 and 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Application Status

Claims 1-18 are pending in the application.

Applicants' election with traverse of Group XVI, claims 1-10 and 15-18 in Paper No. 14, filed 04/15/02 is acknowledged. Applicants' amendment to the specification in Paper No. 15, filed 04/22/02 is acknowledged.

Election/Restrictions

1. Applicants traverse the restriction requirement on the grounds that because the claims of Groups I-XVI have the same classification, co-examination of all claims of Groups I-XVI would not constitute a serious burden on the examiner. Applicant's argument has been fully considered, but is not found persuasive. A search of each of Groups I-XVI would require independent considerations that would require the examiner to focus on different features of each invention that entail differently structured text and sequence searches for both patent and non-patent literature for each of the Groups. Therefore, because each of the patentably distinct inventions listed as Groups I-XVI requires a separate search, restriction for examination purposes is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Sequence Compliance

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May

15, 1990). It is particularly noted that all sequences disclosed in the specification have not been properly identified by SEQ ID NO: (see for example, page 75, line 4 and all other instances in the specification).

Specification/Informalities

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "Method for Accelerating the Rate of Mucociliary Clearance Using Kunitz-Type Serine Proteases". See MPEP § 606.01.

4. The specification is objected to because of the presence of blanks in the text, at for example, pages 71 and 72. Applicant is advised to fill in blanks with the appropriate information.

Claim Objections

5. Claims 16-18 are objected to as being dependent upon non-elected claims. It is suggested that applicants remove the non-elected claims from claims 16-18.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-10 and 15-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. The term "accelerating the rate" in claim 1 (claims 2-10 and 15-18 dependent therefrom) is unclear absent a statement defining to what the expression level is being compared. The term "accelerating the rate" is a relative term and the claim should define and clearly state as to what the accelerated rate of mucociliary clearance is being compared.

8. Claim 18 is confusing in the recitation of "CYS106-CYS156, CYS-115-CYS139, and CYS131-CYS152" as the peptide of SEQ ID NO:8 has only 92 amino acids. It is suggested that applicants clarify the meaning of the claims.

9. Claim 18 is indefinite in the recitation of "native human placental bikunin" as it is unclear as to the amino acid sequence of a "native human placental bikunin". It is suggested that, for example, applicants clearly identify the sequence of "native human placental bikunin" by reference to a specific SEQ ID NO:.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 (claims 2-10 dependent therefrom) are drawn to a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject an effective amount of a genus of Kunitz-type serine protease inhibitors. The specification teaches the structure of only a single representative species of such an inhibitor, i.e., SEQ ID NO:8. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding being a Kunitz-type serine protease inhibitor. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

11. Claims 1-10, 17, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject an effective amount of the peptide of SEQ ID NO:8 as an aerosol to the lungs and optionally having disulfide bonds between CYS20-CYS44 and CYS36-CYS5, does not reasonably provide enablement for a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject by *any* method to *any* tissue an effective amount of *any* Kunitz-type serine protease inhibitor (claim 1) or SEQ ID NO:8 with *any* intra-chain CYS-CYS disulfide bond (claim 17), or with intra-chain disulfide bonds at CYS106-CYS156, CYS-115-CYS139, and CYS131-CYS152 (claim 18). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1 (claim 10 dependent therefrom), 2, 3, 4 (claims 5-9 dependent therefrom), 17, and 18 are so broad as to encompass a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject by *any* method to *any* tissue an effective amount of *any* Kunitz-type serine protease inhibitor or SEQ ID NO:8 with *any* intra-chain CYS-CYS disulfide bond or with intra-chain disulfide bonds at CYS106-CYS156, CYS-115-CYS139, and CYS131-CYS152. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of Kunitz-type serine protease inhibitors, methods and sites of administration and SEQ ID NO:8 with intra-chain disulfide bonds broadly encompassed by the claims. Since the amino acid sequence of a protein determines its therapeutic efficacy, predictability of which

changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject an effective amount of the peptide of SEQ ID NO:8.

While peptide screening techniques are known, it is not routine in the art to screen *all* Kunitz-type serine protease inhibitors or *all* intra-chain disulfide bonds of SEQ ID NO:8 for mucociliary clearance in *any* tissue by *any* method. The positions within an efficacious peptide sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject by *any* method to *any* tissue an effective amount of *any* Kunitz-type serine protease inhibitor or SEQ ID NO:8 with *any* intra-chain CYS-CYS disulfide bond or with intra-chain disulfide bonds at CYS106-CYS156, CYS-115-CYS139, and CYS131-CYS152 because the specification does not establish guidance for using *any* Kunitz-type serine protease inhibitor to accelerate the rate of mucociliary clearance by *any* method to *any* tissue as it is highly unpredictable as to whether *any* Kunitz-type serine protease inhibitor administered by *any* method to *any* tissue will accelerate the rate of mucociliary clearance or guidance as to which of the many intra-chain disulfide bonds of SEQ ID NO:8 will accelerate the rate of mucociliary clearance.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims

broadly including a method of accelerating the rate of mucociliary clearance in a subject in need of such treatment comprising administering to the subject by *any* method to *any* tissue an effective amount of *any* Kunitz-type serine protease inhibitor or SEQ ID NO:8 with *any* intra-chain CYS-CYS disulfide bond or with intra-chain disulfide bonds at CYS106-CYS156, CYS-115-CYS139, and CYS131-CYS152. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re* Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re* Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

12. All claims are rejected. No claims are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX number for this Group is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman, Ph.D.

NASHAAT T. NASHED PHD.
PRIMARY EXAMINER